INPLASY

Efficacy and Safety of Intravitreal Conbercept Combined With Traditional Chinese Medicine for Diabetic Macular Edema: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 June 2025 and was last updated on 21 August 2025.

INTRODUCTION

Review question / Objective The efficacy and safety of intravitreal injection of conbercept (IVC) combined with traditional Chinese medicine (TCM) in patients with diabetic macular edema (DME) remain uncertain.

Condition being studied Diabetic macular edema (DME) is one of the leading causes of vision loss in patients with diabetes (1).The pathogenesis of DME is complex, with inflammation and oxidative stress considered key mechanisms (2).Epidemiological investigations indicate that approximately one in three patients with diabetes develops DR, and the incidence of DME among DR patients can reach 7% (3). Patients with DME frequently experience blurred vision, central visual impairment, and metamorphopsia, significantly impacting their quality of life (4). Currently, clinical treatments for this condition include laser therapy and intravitreal injection of anti-angiogenic agents, aiming to reduce macular edema, prevent vascular leakage, and repair retinal tissue to improve vision (5). However, laser and surgical treatments may cause complications such as retinal atrophy, decreased color perception, choroidal neovascularization, and retinal scarring (6). In addition, repeated intravitreal injections increase the risks of cataract surgery and glaucoma medication, and may also result in intraocular hemorrhage, infection, retinal detachment, and corneal scarring (7). Therefore, identifying safe and effective treatment strategies for DME remains a major focus in clinical practice.

Anti-VEGF agents are the primary treatment for DME (8).Numerous clinical studies have shown that intravitreal conbercept (IVC) injections significantly enhance visual acuity and central macular thickness (CMT) in DME patients, while maintaining a favorable safety profile (9). Traditional Chinese medicine (TCM) has advantages in regulating inflammation, improving microcirculation, and reducing oxidative stress, and has been applied as an adjunctive therapy in fundus diseases (10). This study evaluated the efficacy and safety of combining conbercept with

TCM versus using conbercept alone for treating DME, offering data support for clinical decisions.

METHODS

Search strategy The search strategy utilized a combination of Medical Subject Headings (MeSH) and free-text terms, focusing on primary keywords such as 'Conbercept' or 'KH902,' 'Traditional Chinese Medicine,' 'intravitreal injection,' and 'diabetic macular edema,' with Boolean operators 'AND' and 'OR' used as needed.

Participant or population DME patients.

Intervention Intervention with IVC and TCM, with control receiving IVC only.

Comparator PPV + IVCs (intraoperatively).

Study designs to be included This study was conducted as a systematic review and meta-analysis of randomized controlled trials (RCTs). PubMed, Embase, and Web of Science were systematically searched, supplemented by manual searches of references and clinical studies. Eligible trials compared intravitreal conbercept (IVC) combined with Chinese medicine versus IVC monotherapy. The primary outcomes were overall efficacy, best corrected visual acuity (BCVA) at 1 and 3 months, central macular thickness (CMT) at 1 and 3 months, and safety (adverse events). Risk of bias was assessed using the Cochrane Risk of Bias tool (ROB2), and publication bias was evaluated with Egger's and Begg's tests. Pooled risk ratios (RR) or mean differences (MD) with 95% confidence intervals (CI) were calculated using fixed-effect or random-effect models. Heterogeneity was assessed with the I^2 statistic.

Eligibility criteria RCTs.

Information sources The data for this study were obtained from a comprehensive literature search by systematically searching three major electronic databases, PubMed, EMBASE, and the Cochrane Library (as of August 11, 2022), using the keyword combinations "diabetic retinopathy" and "Conbercept" for screening. In addition, reference lists of eligible studies and relevant review articles were manually searched to ensure completeness of literature coverage. The final literature included in the analysis was limited to the full text of randomized controlled trials (RCTs) and excluded studies that were repetitively published and did not specify the dosage of compazine (IVC) or combination of other medications. All search processes and screening results strictly followed the PRISMA-NMA guidelines.

Translated with DeepL.com (free version).

Main outcome(s) Outcomes included CMT at 1 and 3 months post-surgery, best-corrected visual acuity (BCVA) measured in LogMAR, overall efficacy rate, and adverse events (AEs).

Additional outcome(s) Outcomes included CMT at 1 and 3 months post-surgery, best-corrected visual acuity (BCVA) measured in LogMAR, overall efficacy rate, and adverse events (AEs).

Quality assessment / Risk of bias analysis Risk of bias was assessed using the Cochrane Collaboration's revised RoB2 tool to critically evaluate all included randomized controlled trials (RCTs), focusing on the following core areas: (1) reasonableness of the randomization process (only 7 studies reported the randomization method in full); (2) risk of deviation from the intervention regimen; (3) completeness of the endpoints data (4 studies were rated as high-risk due to missing data) ; (4) objectivity of outcome measures; and (5) risk of selective reporting (all studies showed low risk in this category).

Strategy of data synthesis Data synthesis was performed using Review Manager and Stata software. For dichotomous outcomes, pooled risk ratios (RR) with 95% confidence intervals (CI) were calculated; for continuous outcomes, mean differences (MD) with 95% CI were used. Heterogeneity among studies was assessed using the Chi-square test and quantified with the I^2 statistic, with $I^2 > 50\%$ indicating substantial heterogeneity. A fixed-effect model was applied when heterogeneity was low ($I^2 \leq 50\%$), while a random-effect model was used in cases of significant heterogeneity ($I^2 > 50\%$). Potential sources of heterogeneity were further explored by sensitivity analysis and, if applicable, subgroup analysis. Publication bias was evaluated using funnel plots as well as Egger's and Begg's tests.

Subgroup analysis None.

Sensitivity analysis

Data completeness validation

Studies with missing data on key outcomes (4 high-risk-of-bias studies) were re-analyzed after exclusion to ensure that results were not affected by missing data.

Sources of inconsistency were detected by node splitting for direct versus indirect comparisons

(inconsistency modeling was used if there was significant inconsistency in BCVA).
Covariate Balance Tests
Balance across comparisons of baseline characteristics (duration of diabetes, age, etc.) between groups was assessed (Supplementary Table 2) to confirm that the network met the assumption of transmissibility.
Subgroup analyses of the potential impact of PPV surgical modality (23G/25G/27G) were performed (not achieved due to insufficient sample size, listed as a limitation).
Statistical model sensitivity
A random effects model was used to cover clinical heterogeneity, and 95% confidence intervals were reported for all outcomes.
Ranking probability assessment: comparison of SUCRA values revealed that even between groups with no statistically significant differences (e.g., MI vs Perioperative IVC postoperative hemorrhage), clinical ranking still showed MI to be superior (SUCRA:77.9% vs 59.4%).
Publication Bias Detection
The small sample effect was visually tested by comparing corrected funnel plots (Supplementary Figure 3), which were symmetrical for all outcomes and did not support significant publication bias.

Country(ies) involved China, Sichuan.

Keywords Conbercept; Diabetic macular edema; ; Meta-analysis; Traditional Chinese medicine.

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